

REMARKS

The specification has been amended to remove the dash at the beginning of line 22 on page 15. Claims 30, 36, and 37 have been amended to correct typographical errors. Claim 84 has been amended to make it conform to claims 30 *et al.* No new matter has been added by these amendments.

New claims 89-94 have been added directed to non-nucleic acid antigens and proteinaceous antigens. The specification states at p. 5, ll. 6-8 that the antigens used in the invention are any of those customarily used in vaccine compositions. As the types of such antigens were long and well known to those skilled in the art at the time of filing the present application, it is clear that the applicants had possession of non-nucleic acid antigens and proteinaceous antigens. Accordingly, these claims add no new subject matter.

The foregoing amendments obviate the objections to the specification and claims.

Interview Summary

The applicants gratefully acknowledge the Interview conducted between the undersigned and Examiners Lucas and Housel. The summary of the interview as reflected in the Interview Summary mailed by the PTO on July 28, 2003, is fair and accurate, and the applicants can add nothing more.

Rejections under 35 U.S.C. § 112, second paragraph

Claim 34 has been amended change the proportion of 20% (*i.e.*, ratio of 80%:20%) to a ratio of 4:1. Thus, no new matter is added by this amendment.

Claim 28 has been amended to insert the word "an" before "influenza antigen," as suggest by the Examiner.

Claims 31, 32, 61, 84, 85, and 86 have been canceled, thereby obviating all rejections of these claims.

Claim 75 has been amended to recited administration of the composition of claim 30, and claims 80-82 have been amended to recite the composition rather than amphipathic adjuvant compound, thereby obviating the rejections as to these claims.

In view of the foregoing, the applicants respectfully request reconsideration and withdrawal of the § 112, second paragraph, rejections.

Rejections under 35 U.S.C. § 112

Claims 32, 84, and 86 were rejected as non-enabled for other than a vaccine comprising DC-Chol. While the applicants traverse the rejection, in view of the foregoing amendments, this rejection is obviated.

Rejection under 35 U.S.C. § 102(a)

The Office Action rejected claims 30, 31, 34-37, 62, 64, 67, 75, and 78 as anticipated by Hiu *et al.* on the basis that Hiu *et al.* teach transfection of a nucleic acid with a combination of DC-Chol and DOPE, which was alleged to inherently disclose the presently claimed invention. For the following reasons, the applicants respectfully traverse.

The applicants submit herewith an unexecuted Declaration under 37 C.F.R. § 1.131,¹ which demonstrates that

- a) in France, before November 1994, an adjuvanting amount of DC-Chol and an antigen (influenza HA) were combined and administered to mice to induce an immune response; and
- b) a report completely describing these activities was transmitted to the United State before November 1994.

Thus, the Rule 131 Declaration demonstrates that a species of the presently claimed invention was reduced to practice before November 1994 and introduced into the United States by the inventors before November 1994, the publication date of Hui *et al.* Accordingly, Hui *et al.* is not prior art to the present application.

In addition, the DNA taught by Hui *et al.* is not an antigen as that term is used in the specification and claims. The Examiner acknowledged that in Hui *et al.* the specific immune response is to the peptide encoded by the DNA, concluding that the DNA was, therefore, an antigen. But this interpretation is inconsistent with how the term "antigen" is generally used in the art and, in particular, used in the

¹ The applicants intend to submit an executed Declaration shortly.

present specification. The present specification uses the term as it is defined, for example, in the Oxford Dictionary of Biochemistry and Molecular Biology (A.D. Smit, Ed., Oxford University Press 1997): "any agent that, when introduced into an immunocompetent animal, stimulates the production of a specific **antibody or antibodies that can combine with the antigen.**" (Emphasis added.) For example, at page 1, l. 7 *et seq.*, the specification states:

There are a large number of antigens which, when injected into animals, will cause a production of anti-bodies which are specific to them. One of the principles of vaccination is to stimulate antibody production by the body of a man or an animal by administering chosen antigens thereto. The antibodies thus produced will then enable the body to defend itself against a subsequent infection. However, some antigens do not bring about sufficient stimulation of the immune system when they are administered alone. Hence an adjuvant which will enable the body's immune response to be increased has to be added to them in order to obtain a sufficient amount of antibody to be protective

...

There is hence a need to be able to have adjuvants at one's disposal which enable the immunogenicity of the antigens administered in a vaccine composition to be increased, without any risk of toxicity.

In addition, it is advantageous to have adjuvants at one's disposal which are capable of inducing an immune response that manifests itself in a production of secretory antibodies, such as IgAs.

To this end, the invention provides for the use of an amphipathic compound comprising a lipophilic group derived from a sterol linked to a cationic group, for the production of a vaccine composition.

Hence, the specification characterizes antigens for use in the composition of the invention as those that elicit antibodies that combine with the antigen.

Hui *et al.* does not teach or suggest the combination of an adjuvanting amount of DC-Chol with an antigen that induces secretory antibodies that combine with the antigen. Hui *et al.* teaches DC-Chol cationic liposomes carrying the H-2K^b gene or CMV-Luciferase DNA and report detection of anti-H-2K^b **protein** antibodies following *in vivo* immunization to mouse spleens with the liposomes. Hui *et al.* does not teach that antibodies were generated against the H2K^b gene DNA. Hence, the DNA of Hui *et al.* is not an antigen as that term is used in the present specification and claims.

DNA does not necessarily induce a secretory antibody response to itself. Enclosed with this response are copies of publications by Le *et al.* (*Vaccine* **18**, 1893 (2000)) and MacGregor *et al.* (*J.*

Infect. Diseases **178**, 92 (1998)). Both publications disclose the results of *in vivo* administration of DNA-based vaccines and report that no anti-DNA antibodies were observed.

Corresponding to the failure to teach anti-DNA antibodies, Hui *et al.* fails to teach an adjuvanting effect by the DC-Chol and therefore fails to teach an amount of DC-Chol that serves as an adjuvant. That is, Hui *et al.* fails to teach that the amount of DC-Chol was an adjuvanting amount for the purported "antigen."

As Hui *et al.* fails to teach an antigen according to the invention and fails to teach an adjuvanting amount of DC-Chol for use with the antigen, Hui *et al.* cannot anticipate the present claims.

In view of the foregoing, the applicants respectfully request reconsideration and withdrawal of this § 102 rejection.

Rejection under 35 U.S.C. § 103

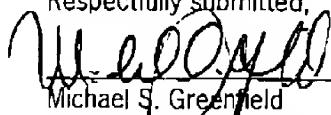
The Office Action maintained the rejection of the claims as obvious, dismissing the applicants' previously submitted arguments on the basis that claim 30 had been amended to the word "adjuvant." The applicants respectfully traverse. Whether the word adjuvant is recited in the claim is irrelevant because, as the Examiner noted with regard to the Hui *et al.*, the DC-chol would inherently act as an adjuvant. Nevertheless, the applicants have amended claim 30 to recite that the claimed composition comprise an "adjuvanting" amount of DC-chol, thereby removing ambiguity.

In view of the foregoing, the applicants respectfully request reconsideration and withdrawal of this § 103 rejection.

If there are any questions or comments regarding this Response or application, the applicants encourage the Examiner to contact the undersigned attorney as indicated below.

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Respectfully submitted,


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